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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,677	03/24/2000	SVEND BIRKELUND	BIRKELUND=1	2720

1444 7590 01/23/2003

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EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	15

DATE MAILED: 01/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/446,677	BIRKELUND ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2002 and 10 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13 and 15-18* is/are pending in the application.

4a) Of the above claim(s) *1-4, 6, 8, 9, 11, 13 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *24* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicants' amendment D and response received October 03, 2002, paper 23 is acknowledged. Claims 5, 7 and 10 were amended. Claim 12 was canceled. New claim 18 was added. Priority statement on page 1 of the specification was inserted.

2. Applicants' supplemental information disclosure statement, received December 10, 2002, paper 24 is acknowledged.

3. Currently claims 1-11, 13 and 15-18 are pending.

4. Claims 5, 7, and 10 are under consideration. Claims 1-4, 6, 8, 9, 11, 13 and 15-18 are withdrawn from consideration as being drawn to non-elected inventions.

Prior Citations of Title 35 Sections

5. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Objections Maintained

6. Objections to drawing made in paragraph 8 of the office action mailed June 03, 2002 (paper number 22) are maintained. No corrections were sent by the applicants. However applicants noted in their response that they are in the process of procuring necessary full tone photographic prints and they will be filed in due course.

Rejections Moot

7. The rejection of claim 12 under 35 USC § 101, made in paragraph 11of the office action mailed June 03, 2002 (paper number 22) is moot in view of applicants' cancellation of the claim.

8. The rejection of claim 12 under 35 USC § First Paragraph, made in paragraph 12 of

the office action mailed June 03, 2002 (paper number 22) is moot in view of applicants' cancellation of the claim.

9. The rejection of claim 12 under 35 USC § Second Paragraph, made in paragraph 13 of the office action mailed June 03, 2002 (paper number 22) is moot in view of applicants' cancellation of the claim.

10. The rejection of claim 12 under 35 USC § 102 (b), made in paragraph 17 of the office action mailed June 03, 2002 (paper number 22) is moot in view of applicants' cancellation of the claim.

Rejections Withdrawn

11. The rejection of claim 5 under 35 USC § 101, made in paragraph 11 of the office action mailed June 03, 2002 (paper number 22) is withdrawn in view of applicants' amendment of the claim.

12. The rejection of claims 5, 7 and 10 under 35 USC § Second Paragraph, made in paragraph 13 of the office action mailed June 03, 2002 (paper number 22) is withdrawn in view of applicants' amendment of the claims.

Rejections Maintained

13. The rejection of claims 5, 7 and 10 under 35 USC § First Paragraph, made in paragraph 12 of the office action mailed June 03, 2002 (paper number 22) is maintained.

The rejection was as stated below:

Claims 5, 7 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for the variants and subsequences claimed. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims are directed to a protein derived from *Chlamydia pneumoniae* having amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof. The claims are broad and encompass any protein derived from Chlamydia *pneumoniae.* The specification indicates that "a variant will typically show a sequence similarity of preferably at least 50%, preferably at least 60%, preferably at least 70%, such as at least 80%, e.g. at least 90%, 95%, 98%." (see page 10, lines 10-14). The specification further indicates, " A subsequence will typically comprise at least 100 amino acids, preferably at least 80 amino acids, more preferably at least 70 amino acids, such as 50 amino acids. It might be as small as 10-50..." (see page 10 lines 29-34).

The specification does not provide any description of these variants and which positions in these variants can be altered without loss of protein activity or which position would render a non-functional protein. Furthermore, no examples of any of these variants are provided. No information, beyond the characterization of SEQ ID NO: 2 have been provided by applicant, which would indicate possession of the claimed variants. No description has been provided by applicant of the variants encompassed by the claims. The specification has no disclosure of the function of all of the variants. Each variant and subsequences of the proteins claimed is a large variable genus, which can have a wide variety of functions. The art also teaches functionally unrelated molecules can be produced by these substitutions for example Van de Loo et al. (Proc. Natl. Acad. Sci 1995) teaches that polypeptides of approximately 67% homology to a desaturase from Arabidopsis were found to be hydrolases once tested for activity (see abstract). Similarly, Broun et al. (Science 1998) teaches that as few as four amino acid substitutions can convert an

oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform an hydrolase into a desaturase (see abstract). Therefore, many functionally unrelated variants (polypeptides) are encompassed within the scope of the claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variants broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of prediction protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. Multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does **not** disclose the following:

- the general tolerance to modification and extent of such tolerance;

- specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which retain the biological activity if the intact protein; and
- the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicant have **not** provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed protein in manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the proteins structure and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen Inc v. Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed.Cir.1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S.P.Q. 546(Bd. Pat. App. & Int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the invention commensurate in scope with the claims.

Applicants' arguments filed October 03, 2002 have been fully considered and are not persuasive.

Applicants argue " We have amended the claims to recite that the variants have a minimum amino acid sequence identity of 80% to the recite polypeptides. In this regard, it should be noted that the typical sequence identities among the recited polypeptides, which are of similar biological function, are in the range of 53% - 66%". The applicants further argue that " The examiner has acknowledged that the "80%" limit is taught on page 10". Applicants also argue " While the claims do not specify the particular amino acid positions at which mutation is allowed, or the replacement amino acids for each such position, we believe that these choices are reasonably left to those skilled in the art."

It is the examiner's position that the specification does not reasonably provide enablement for the variants and subsequences in the amended claims. The specification does not provide any description of these variants and which positions in these variants can be altered without loss of protein activity or which position would render a non-functional protein. Furthermore, no examples of any of these variants are provided. The examiner respectfully disagree with the applicants that these choices are reasonably left to those skilled in the art. Protein chemistry is probably one of the most unpredictable areas of biotechnology. Rudinger et al teach "particular amino-acids and sequences for different aspects of biological activity can not be predicted a priori but must be determined case to case by painstakingly experimental study" (see page 6). Salgaller et al teach modifications (i.e. mutations, substitutions, deletions) of the amino acid structure of peptide can alter the activity of the protein. In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives and fragments encompassed in the scope of the claims one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention. These references demonstrate that modification (i.e. mutations, substitutions, deletions), will often dramatically affect the biological activity of a protein.

In conclusion the specification does not support the broad scope of the claims, which encompass a multitude of analogs or equivalents because the specification does not disclose the following:

-the general tolerance to modification and extent of such tolerance;

-specific positions which can be predictably modified; and

-the specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims broadly including any number of variants. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

14. The rejection of claim 5 under 35 USC § 102(b), made in paragraph 14 of the office action mailed June 03, 2002 (paper number 22) is maintained.

The rejection was as stated below:

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993). Prior art already made of record.

Claim 5 is drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 50% and similar biological function.

Melgosa et al. teach a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract and page 202). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa protein taught by Melgosa et al.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed October 03, 2002 have been fully considered and are not persuasive.

Applicants argue " Melgosa et al. teach a single protein of 98-kDa from the outer membrane complex of *Chlamydia pneumonia.* The last words of said reference states " further molecular and antigenic studies of the 98-kDa will help to understand the role of this protein in structure as well as pathogensis of *Chlamydia pneumonia".* Thus, by studying Melgosa et al. a person skilled in the art would not have been lead to conclude that the gel band disclosed by Melgosa et al. in fact contained several different proteins". Applicants further argue " In face, the present invention is based upon further studies of the protein of Melgosa et al." Applicants also argue "

At that time further molecular and antigenic studies of the 98-kDa band were not readily possible." Applicants further argue, " Thus, the inventive step of the present invention relates to the discovery by the present inventors that the gel band did contain more that one protein and thus the cloning and sequencing of some of said novel proteins."

In response to applicants' argument that the reference fails to show certain features of applicants' invention, it is noted that the features upon which applicant relies (i.e., several different proteins) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicants' argument that the inventive step of the present invention relates to the discovery by the present inventors that the gel band did contain more that one protein, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In conclusion, it is the examiner's position that claim 5 as amended is still drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 80%. The prior teach the claimed protein.

15. The rejection of claim 7 under 35 USC § 102(b), made in paragraph 15 of the office action mailed June 03, 2002 (paper number 22) is maintained.

The rejection was as stated below:

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993).

Claim 7 is drawn to a kit for diagnosis of infection of a mammal with *Chlamydia pneumoniae* comprising a protein with the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof. (The examiner views the claimed kit as a product or a composition comprising a protein of *Chlamydia pneumoniae*).

Melgosa et al. teach a product or a composition for diagnosis of infection of a mammal with *Chlamydia pneumoniae* comprising a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a composition of 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract) This composition was used for diagnosis of Chlamydia *pneumoniae* in rabbits (see page 201). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa-protein composition taught by Melgosa et al.

Applicants' arguments filed October 03, 2002 have been fully considered and are not persuasive.

Applicants argue " Melgosa et al. teach a single protein of 98-kDa from the outer membrane complex of *Chlamydia pneumonia.* The last words of said reference states " further molecular and antigenic studies of the 98-kDa will help to understand the role of this protein in structure as well as pathogenesis of *Chlamydia pneumonia".* Thus, by studying Melgosa et al. a person skilled in the art would not have been lead to conclude that the gel band disclosed by Melgosa et al. in fact contained several different proteins". Applicants further argue " In face, the present invention is based upon further studies of the protein of Melgosa et al." Applicants also argue " At that time further molecular and antigenic studies of the 98-kDa band were not readily possible." Applicants further argue " Thus, the inventive step of the present invention relates to

the discovery by the present inventors that the gel band did contain more that one protein and thus the cloning and sequencing of some of said novel proteins."

In response to applicants' argument that the reference fails to show certain features of applicants' invention, it is noted that the features upon which applicant relies (i.e., several different proteins) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicants' argument that the inventive step of the present invention relates to the discovery by the present inventors that the gel band did contain more that one protein, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In conclusion, it is the examiner's position that the base claim (claim 5) which claim 7 is depended from is drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 80%. The prior teach the claimed invention.

16. The rejection of claim 10 under 35 USC § 102(b), made in paragraph 16 of the office action mailed June 03, 2002 (paper number 22) is maintained.

The rejection was as stated below:

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993).

Claim 10 is drawn to a composition for immunizing a mammal against *Chlamydia pneumoniae* comprising a protein with the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof.

Melgosa et al. teach a composition for immunizing a mammal against *Chlamydia pneumoniae* comprising a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a composition of 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract) This composition was used to immunize rabbits (see page 200). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa-protein composition taught by Melgosa et al.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed October 03, 2002 have been fully considered and are not persuasive.

Applicants argue " Melgosa et al. teach a single protein of 98-kDa from the outer membrane complex of *Chlamydia pneumonia.* The last words of said reference states " further molecular and antigenic studies of the 98-kDa will help to understand the role of this protein in structure as well as pathogensis of *Chlamydia pneumonia".* Thus, by studying Melgosa et al. a person

skilled in the art would not have been lead to conclude that the gel band disclosed by Melgosa et al. in fact contained several different proteins". Applicants further argue " In face, the present invention is based upon further studies of the protein of Melgosa et al." Applicants also argue " At that time further molecular and antigenic studies of the 98-kDa band were not readily possible." Applicants further argue, " Thus, the inventive step of the present invention relates to the discovery by the present inventors that the gel band did contain more that one protein and thus the cloning and sequencing of some of said novel proteins."

In response to applicants' argument that the reference fails to show certain features of applicants' invention, it is noted that the features upon which applicant relies (i.e., several different proteins) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicants' argument that the inventive step of the present invention relates to the discovery by the present inventors that the gel band did contain more that one protein, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In conclusion, it is the examiner's position that the base claim (claim 5) which claim 10 is depended from is drawn to a composition a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 80%. The prior teach the claimed protein.

Conclusion

17. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

January 16, 2003

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